

We claim:

1. A method for synthesis of a product polypeptide, comprising:
 - (a) preparing a multiphase solvent mixture, wherein the solvent mixture comprises at least one organic solvent;
 - (b) adding a first polypeptide comprising a first amino acid having a first unprotected reactive group;
 - (c) adding a ligation label comprising a second amino acid having a second unprotected reactive group; and
 - (d) collecting the product polypeptide formed by a reaction between the first polypeptide with the ligation label;wherein the first unprotected reactive group and the second unprotected reactive group react to form a covalent bond between the first unprotected reactive group and the second unprotected reactive group.
2. The method of claim 1, wherein the multiphase solvent mixture is a two phase mixture.
3. The method of claim 2, wherein the multiphase solvent mixture comprises at least two component solvents, wherein one of the at least two component solvents exhibits a dielectric strength of 4 to 12 while another of the at least two component solvents exhibits a higher dielectric strength.
4. The method of claim 1, wherein the multiphase solvent mixture is an emulsion.
5. The method of claim 4, wherein the multiphase solvent mixture further comprises an emulsifier.
6. The method of claim 5, wherein the emulsifier is selected from the group consisting of phospholipids, block copolymers, and mixtures thereof.

7. The method of claim 1, wherein the first polypeptide is selected to have a sequence of membrane-incorporated polypeptide segment.

8. The method of claim 7, wherein the ligation label is a second polypeptide and wherein the second polypeptide is selected to have a sequence of membrane-incorporated polypeptide segment.

9. The method of claim 8, wherein the first polypeptide is selected from the group consisting of a membrane polypeptide, a transmembrane polypeptide, a receptor and useful fragments thereof.

10. The method of claim 9, wherein the first polypeptide and the second polypeptide are portions of a G-protein coupled receptor, and the linked polypeptides form a larger portion of the G-protein coupled receptor.

11. The method of claim 1, wherein the multiphase solvent mixture comprises at least two organic solvents.

12. The method of claim 11, wherein the multiphase solvent mixture comprises DMF and octanol.

13. A method for chemoselective chemical ligation of a product polypeptide, comprising:

- (a) preparing a multiphase solvent mixture, comprising at least one organic solvent;
- (b) adding a first polypeptide comprising a first amino acid having a first unprotected reactive group;
- (c) adding a ligation label comprising a second amino acid having a second unprotected reactive group; and,
- (d) collecting the product polypeptide formed by a reaction between the first polypeptide with the ligation label;

wherein the first unprotected reactive group undergoes chemoselective chemical ligation with the second unprotected reactive group to form a covalent bond between the first unprotected reactive group and the second unprotected reactive group.

14. The method of claim 13, wherein the chemoselective ligation is selected from the group of native chemical ligation, oxime-forming ligation, thioester-forming ligation, thioether-forming ligation, hydrazone-forming ligation, thiazolidine-forming ligation and oxazolidine-forming ligation.

15. The method of claim 14, wherein the first polypeptide is selected to have a sequence of membrane-incorporated polypeptide segment.

16. The method of claim 13, wherein the multiphase mixture is a two phase mixture.

17. The method of claim 16, wherein the multiphase solvent mixture comprises at least two component solvents, wherein one of the at least two component solvents exhibits a dielectric strength of 4 to 12 while another of the at least two component solvents exhibits a higher dielectric strength.

18. The method of claim 13, wherein the multiphase solvent mixture is an emulsion.

19. The method of claim 18, wherein the multiphase solvent mixture further comprises an emulsifier.

20. The method of claim 19, wherein the emulsifier is selected from the group consisting of phospholipids, block copolymers, and mixtures thereof.

21. The method of claim 13, wherein the first polypeptide is selected to have a sequence of membrane-incorporated polypeptide segment.

22. The method of claim 21, wherein the ligation label is a second polypeptide and wherein the second polypeptide is selected to have a sequence of membrane-incorporated polypeptide segment.

23. The method of claim 22, wherein the first polypeptide is selected from the group consisting of a membrane polypeptide, a transmembrane polypeptide, a receptor and useful fragments thereof.

24. The method of claim 23, wherein the first polypeptide and the second polypeptide are portions of a G-protein coupled receptor, and the linked polypeptides form a larger portion of the G-protein coupled receptor.

25. The method of claim 13, wherein the multiphase solvent mixture comprises at least two organic solvents.

26. The method of claim 25, wherein the multiphase solvent mixture comprises DMF and octanol.

27. A method of assembling polypeptide segments, comprising:
(a) preparing a multi-phase solvent mixture, comprising at least one organic solvent;
(b) adding a first polypeptide comprising a first amino acid having a first unprotected reactive group;
(c) adding a second polypeptide comprising a second amino acid having a second unprotected reactive group; and,
(d) collecting the product polypeptide formed by a reaction between the first polypeptide with the ligation label;
wherein the first unprotected reactive group and the second unprotected reactive group react to form a covalent bond between the first unprotected reactive group and the second unprotected reactive group.

28. A chemical intermediate composition, comprising:
(a) a multiphase solvent mixture, comprising at least two component solvents, wherein one of the at least two component solvents exhibits a dielectric strength of 4 to 12 while another of the at least two component solvents exhibits a higher dielectric strength and wherein at least one of the at least two component solvents is an organic solvent;
(b) a first polypeptide comprising a first amino acid having a first unprotected reactive group; and,

(c) a ligation label comprising a second amino acid having a second unprotected group.

29. A composition, comprising:

(a) a multiphase solvent mixture, wherein the solvent mixture comprises at least one organic solvent;

(b) a first polypeptide comprising a first amino acid having a first unprotected reactive group;

(c) a ligation label comprising a second amino acid having a second unprotected group; and,

(d) a product polypeptide formed by a reaction between the first polypeptide with the ligation label;

wherein the first unprotected reactive group and the second unprotected reactive group react to form a covalent bond between the first unprotected reactive group and the second reactive group.